

REMARKS

Reconsideration of the application is requested.

Claims 120-131 are now in the application. Claims 120-131 are subject to examination. Claims 120-131 have been added. Claims 58-119 have been canceled to facilitate prosecution of the instant application. Claims 1-57 were canceled in a preliminary amendment.

Under the heading "Specification" on page 2 of the above-identified Office Action, the Examiner objected to the specification for failing to provide proper antecedent basis for the claimed subject matter.

The terms, "at least one conical nipple", "measuring heads", and "external form" no longer appear in the claims. Page 26 of the specification has been amended to refer to a rectangular shaped magnet holder. Support for the change can be found by referring to original claim 47. Page 11 of the specification has been amended to refer to the poles. Support for the change can be found by referring to original claims 36, 45, 47, and 48.

Under the heading "Claim Rejections – 35 USC § 102" on page 3 of the above-identified Office Action, claims 70, 71 and 86 have been rejected as being fully anticipated by German Patent No. DE 19808055 A1 to Adamietz et al. under 35 U.S.C. § 102.

New claims 120-131 have been presented. Support for the new claims can be found by referring to the previous claims and to the specification in the following manner:

New claim	previously presented claim(s)
120	70, 74, 94, and examples 5, 6, and 10
121	108
122	109
123	110
124	111
125	78
126	79
127	80
128	85
129	86, 87
130	98
131	104

Applicants believe it is clear that the limitations in new claim 120 are not anticipated by Adamietz et al.

Adamietz et al. do not teach a bioreactor including (i) a basic bioreactor body with a reactor lock connected thereto in a pressure-proof and sterile manner to define therein a reactor chamber, (ii) said reactor chamber comprising (a) a

support surface on a bioreactor floor for a three-dimensional transplant, which is obtained by mixing, suspending to homogeneity and hardening prepared cells with a bio-compatible and bio-degradable carrier structure, and (b) a permanent magnet comprising a mini actuator disposed in the bioreactor chamber situated above said transplant and acting as a vertically oriented and guided pressure applicator or stamp, which is moved vertically and contactless in the bioreactor chamber by externally disposed control and steering magnets, and (iii) at least two hose coupling connectors for feeding and continuous perfusion of the transplant with a medium, wherein the mini actuator with the magnetic core is encapsulated in a biologically inert enveloping body which has vertically oriented flow channels for exact vertical guiding and medium flow optimization at an edge of the enveloping body and fits with its external diameter exactly into the bioreactor chamber with low friction, whereby a diameter of the transplant, which is exactly medially positioned in the bioreactor chamber, is smaller than an external diameter of the magnetic mini actuator.

Applicants also believe that the teachings in Bader (WO 2003/060055) and Takagi et al. (US 2005/0106716) do not anticipate or suggest the claimed invention and will now comment on the teachings therein.

Bader et al. (see Figure 13 and respective disclosure in the specification) disclose a magnetizable disk which is elastically fixed in the upper part of the reactor chamber and can be stimulated. by an electromagnetic coil located in the reactor lock. Thus, the magnetizable disk may carry out only small

movements up and down and thus pressure on the transplant and perfusion movement of the medium are pretty small and have only little impact. Moreover, the disk (25) in Fig. 13 will never have the chance to touch the transplant on the bottom of the bioreactor. Thus, the necessary biological stress on the transplant simulated by the pressure of the vertically moving disk is very limited by this construction.

Takagi et al. use a pressing plate which is located directly (without any remarkable space to the transplant) above the transplant in order to simulate biologically similar forces directed to the transplant. The pressing plate is moved up and down by an electromagnetic unit. The distance of the plate which must be covered is only very little, and therefore, no problems with respect to the moved medium and its flow should be expected. Thus, the plate does not need any means which improve or optimize medium flow during perfusion. In general, the possibility to carry out a satisfying perfusion by inducing respective shearing forces is very limited in the bioreactor of Takagi et al. consisting of a bioreactor chamber with extreme limited dimensions and size.

In bigger reaction chambers, which allow an extensive feeding of and mixing with perfusion media within a short time, the impact of a compact mini actuator which is to be moved over a larger distance within the reactor chamber is unfavorable with respect to the movement and perfusion of the medium, thus providing non-standardized shearing and pressure forces.

Only, the magnetic actuator of the invention that provides flow channels at the edge of the actuator and exactly fits in the cylindrical reactor chamber prevents too high positioning forces and forces to overcome medium resistance.

Moreover, only very exact and permanent vertically directed forces on the transplant initiate a satisfying stress on the cells that is comparable with biological conditions. This problem is solved by the invention in spite of the relatively large dimensions of the bioreactor chamber, which are favorable for providing a sufficient and effective volume. The necessity of an exact geometry of the bioreactor according to the invention under operating conditions is also depicted in Examples 5 and 10.

Under the heading "Claim Rejections – 35 USC § 102" on page 4 of the above-identified Office Action, claims 70, 71, 74, 85, 95 and 119 have been rejected as being fully anticipated by U.S. Publication 2004/0235150 A1 to Takagi et al. under 35 U.S.C. § 102.

Please see the discussion above with regard to claim 120 and the teaching in Takagi et al.

Under the heading "Claim Rejections – 35 USC § 102" on page 5 of the above-identified Office Action, claims 70, 115, 117 and 118 have been rejected as being fully anticipated by U.S. Patent No. 6,121,042 to Peterson et al. under 35 U.S.C. § 102.

Applicants believe it is clear that the limitations in new claim 120 are not anticipated by Peterson et al. Peterson et al. do not teach a bioreactor including (i) a basic bioreactor body with a reactor lock connected thereto in a pressure-proof and sterile manner to define therein a reactor chamber, (ii) said reactor chamber comprising (a) a support surface on a bioreactor floor for a three-dimensional transplant, which is obtained by mixing, suspending to homogeneity and hardening prepared cells with a bio-compatible and bio-degradable carrier structure, and (b) a permanent magnet comprising a mini actuator disposed in the bioreactor chamber situated above said transplant and acting as a vertically oriented and guided pressure applicator or stamp, which is moved vertically and contactless in the bioreactor chamber by externally disposed control and steering magnets, and (iii) at least two hose coupling connectors for feeding and continuous perfusion of the transplant with a medium, wherein the mini actuator with the magnetic core is encapsulated in a biologically inert enveloping body which has vertically oriented flow channels for exact vertical guiding and medium flow optimization at an edge of the enveloping body and fits with its external diameter exactly into the bioreactor chamber with low friction, whereby a diameter of the transplant, which is exactly medially positioned in the bioreactor chamber, is smaller than an external diameter of the magnetic mini actuator.

Under the heading "Claim Rejections – 35 USC § 102" on page 5 of the above-identified Office Action, claims 70, 71, 75, 86, 87 and 94 have been rejected as

being fully anticipated by International Patent No. WO 2003/060055 A1 to Bader under 35 U.S.C. § 102.

Please see the discussion above with regard to claim 120 and the teaching in Bader.

Under the heading “Claim Rejections – 35 USC § 102” on page 6 of the above-identified Office Action, claims 70, 71 and 94 have been rejected as being fully anticipated by U.S. Publication No. 2005/016716 A1 to Takagi et al. under 35 U.S.C. § 102.

Please see the discussion above with regard to claim 120 and the teaching in Takagi et al.

Under the heading “Claim Rejections – 35 USC § 103” on page 7 of the above-identified Office Action, claims 97-100, 102 and 104-108 have been rejected as being obvious over U.S. International Patent No. 2003/060055 to Bader in view of U.S. Patent No. 6,001,643 to Spaulding under 35 U.S.C. § 103.

Even if there would have been a suggestion to combine the teachings in these references, the claimed invention would not have been obtained for the reasons given above with regard to the teaching in Bader and claim 120.

Under the heading “Claim Rejections – 35 USC § 103” on page 10 of the above-identified Office Action, claim 108 has been rejected as being obvious over U.S. Patent No. 6,121,042 to Peterson et al. in view of International Patent No. 2003/060055 to Bader under 35 U.S.C. § 103.

Even if there would have been a suggestion to combine the teachings in these references, the claimed invention would not have been obtained for the reasons given above with regard to the teaching in Bader and claim 120.

Under the heading “Claim Rejections – 35 USC § 103” on page 11 of the above-identified Office Action, claims 76 and 77 have been rejected as being obvious over International Patent No. 2003/060055 to Bader in view of U.S. Patent No. 5,501,971 to Freedman et al. under 35 U.S.C. § 103.

Even if there would have been a suggestion to combine the teachings in these references, the claimed invention would not have been obtained for the reasons given above with regard to the teaching in Bader and claim 120.

Under the heading “Claim Rejections – 35 USC § 103” on page 12 of the above-identified Office Action, claims 78-80 have been rejected as being obvious over International Patent No. 2003/060055 to Bader in view of U.S. Publication No. 2004/0219659 A1 under 35 U.S.C. § 103.



Even if there would have been a suggestion to combine the teachings in these references, the claimed invention would not have been obtained for the reasons given above with regard to the teaching in Bader and claim 120.

Under the heading "Claim Rejections – 35 USC § 103" on page 13 of the above-identified Office Action, claims 109-112 have been rejected as being obvious over U.S. Publication No. 2005/016716 A1 to Takagi et al. in view of U.S. Publication No. 2004/0235250 A1 under 35 U.S.C. § 103.

Even if there would have been a suggestion to combine the teachings in these references, the claimed invention would not have been obtained for the reasons given above with regard to the teaching in Takagi et al. and claim 120.

It is accordingly believed to be clear that none of the references, whether taken alone or in any combination, either show or suggest the features of claim 120. Claim 120 is, therefore, believed to be patentable over the art. The dependent claims are believed to be patentable as well because they all are ultimately dependent on claim 120.

In view of the foregoing, reconsideration and allowance of claims 120-131 are solicited.

In the event the Examiner should still find any of the claims to be unpatentable, counsel would appreciate receiving a telephone call so that, if possible, patentable language can be worked out.

Petition for extension is herewith made. The extension fee for response within a period of two months pursuant to Section 1.136(a) in the amount of \$490.00 in accordance with Section 1.17 is enclosed herewith.

Please charge any other fees that might be due with respect to Sections 1.16 and 1.17 to the Deposit Account of Lerner Greenberg Stermer LLP, No. 12-1099.

Respectfully submitted,

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